NATIONAL MARROW DONOR PROGRAM®

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July 25, 2014

LCDR Christopher Steele
Office of Naval Research
Code 34 – Warfighter Performance
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-13-1-0039 between the Office of Naval Research and the National Marrow Donor Program

Dear LCDR. Steele:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of April 1, 2014 to June 30, 2014.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at cabler@nmdp.org.

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Contracts Manager

Enclosure: Quarterly Report with SF298

C: J. Kabisch – ACO (ONR-Chicago)
Dr. Robert J. Hartzman, CAPT, MC, USN (Ret)
Jennifer Ng, PhD – C.W. Bill Young Marrow Donor Recruitment and Research Program
J. Rike - DTIC (Ste 0944)
NRL (Code 5227)
Dennis Confer, MD, Chief Medical Officer, NMDP
Stephen Spellman, Director, Immunobiology & Observational Research, NMPD

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Spellman, Stephen

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3001 Broadway St., N.E., Ste. 500
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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation: Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE	Same as Report	12	Dennis L. Confer, MD – Chief Medical Office
U	U	U			19b. TELEPONE NUMBER (*Include area code)* 612.362.3425

NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

Grant Award N00014-13-1-0039

DEVELOPMENT OF MEDICAL TECHNOLOGY FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS

QUARTERLY PERFORMANCE / TECHNICAL REPORT

FOR

APRIL 01, 2014 to JUNE 30, 2014

PERIOD 6

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
1-800-526-7809

QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

April 01, 2014 through June 30, 2014

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	Task 5 – Bioinformatics Web Site	Open	N/A
	Task 6 – Utilize Search Strategy Advisors to Improve Algorithm	No Activity	N/A
	Task 7 – Population Genetics	Closed	N/A
	Task 8 – Haplotype Matching	Closed	N/A
	Task 9 – Global Haplotype/Benchmark	Closed	N/A
IIB.4	**Objective 4 – Reduction of Donor Matching Time**		
	Task 1 – Expand Network Communications	Closed	N/A
	Task 2 – Central Contingency Management	No Activity	N/A
	Task 3 – Benchmarking Analysis	Closed	N/A
	Task 4 – Expand Capabilities of Collection and Apheresis Centers	Closed	N/A
IIC.	**Immunogenetic Studies**		
IIC.1	**Objective 1 – Influence of HLA Mismatches**		
	Task 1 – Donor Recipient Pair Project	No Activity	N/A
IIC.2	**Objective 2 – Role of Other Loci and GVHD**		
	Task 1 – Analysis of Non-HLA Loci	Open	7
	Task 2 – Related Pairs Research Repository	Closed	N/A
	Task 3 – CIBMTR Integration	Closed	N/A
IID	**Clinical Research in Transplantation**		
IID.1	**Objective 1 – Clinical Research Improves Outcomes**		
	Task 1 – Observational Research, Clinical Trials and NIH Transplant Center	Open	8
	Task 2 – Research with NMDP Donors	Closed	N/A
	Task 3 – Expand Immunobiology Research	No Activity	N/A
	Acronym List		9

Note: The majority of the effort under this Grant is now being performed under the follow on ONR Grant N00014-14-1-0028. Therefore in order to save space the Tasks that are closed or had no activity during the reporting period, as noted in the Table of Contents above, have been deleted from the Report.

IIA. Contingency Preparedness – Objective 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians

IIA.1 Task 1: *Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event.*

Period 6 Activity:

- Coordinated with the Association of State and Territorial Health Officials on the joint ASTHO – CDC - RITN project to determine the distribution process of the medical countermeasure G-CSF (Neupogen) following a mass casualty radiological incident.

IIB. Rapid Identification of Matched Donors – Objective 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.

IIB.1 Task 1: *Expand the genetic diversity of the Registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies.*

Period 6 Activity:

Laboratory Site Visit:

- Two NMDP staff performed a site visit to a contracted HLA typing laboratory. Operational topics were discussed and presentations given including an overview of the Be The Match Registry, as well as specifics of the lab's service agreement performance and interactions with the NMDP. Likewise, the lab staff gave a reciprocating presentation on the processes and workflows of their HLA typing methodologies, which included a tour of their laboratory facilities and equipment, highlighting recent changes in lab testing platforms and staffing. These discussions are important to allow NMDP to continue to provide low cost and high quality HLA typing for patients searching the registry.

2-Step Recruitment at Live Drive Registration:

- The 2-Step Activation Phase Two Pilot ran from March 28 through August 28, 2013. Phase Two included an online activation channel, in addition to the Phase One channels of phone and text activation.
- An additional email outreach to those who did not activate their membership during the pilot period is in progress.

IIB.1 Task 4: *Evaluate the suitability of buccal swabs as a method to collect DNA samples to HLA type casualties and potential related donors in contingency situations, and to obtain research samples.*

Period 6 Activity:

Frozen Buccal Swab Study:

- The study will compare swabs stored at room temperature and -30°C, for quality of DNA, quantity of DNA, and high resolution HLA characterization, at selected time points over multiple years.
- Sample collection from volunteer donors has been completed. A contract was executed with a lab that will perform Next Generation Sequencing based HLA typing on the stored samples. Collection of fresh baseline samples will be completed next quarter.

Sample Storage Research Study:

- The purpose of this 5 year research study was to evaluate, over time, the quality and quantity of the DNA within three stored sample types: frozen whole blood, whole blood spotted on filter paper (FP) and buccal swabs (SW), both stored at room temperature. Study results were summarized in a previous quarterly progress report.
- The study was presented as a poster at the WMDA IDRC 2014 meeting in London, UK.

IIB. Rapid Identification of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.

IIB 2 Task 1: *Ongoing collection of primary data for validation and storage in the Registry database.*

Period 6 Activity:

Genomic DNA Swabs as a Quality Control sample type:

- 233 existing QC volunteer blood samples with a minimum of 10 frozen aliquots in inventory were shipped for DNA extraction for inclusion in the NMDP blind buccal swab QC program.
  - These represent a 45% increase in overall buccal swab QC inventory, and help achieve at least a 7.5 week unique QC master shipment rotation.
  - Significant cost savings were achieved by switching from B-LCL initiations/cultures/expansions to extracted DNA, enhancing long-term sustainability of the QC program.

- 10 DNA QC Masters extracted during the pilot phase of the study have been incorporated into the blind QC program. No issues were reported by any of the laboratories.

IIB. Rapid Identification of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.

IIB 3 Task 5: *Develop a bioinformatics web site for frequency information.*

Period 6 Activity:

- Bioinformatics, NMDP Security and an external vendor worked together to incorporate the Authorization and Access structure within the NMDP Enterprise Solutions. This team assessed tailored Bioinformatics Research needs. This work is ongoing, with the result being the addition of Authorization and Access to Bioinformatics Research applications so that access can be monitored.

- As part of the work of the Website, and its goal of making it a global hub for HLA informatics and standards, Bioinformatics and an external collaborator have been working to enrich the available HLA Reference Data. The group worked on

applications to make this an open-source solution that will allow interested parties an easier method to access the HLA Reference data.

- Developed user interfaces and tools for the multi-race matching services application for use by the Search Strategy team.

IIC. Immunogenetic Studies – Objective 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.

IIC.2 Task 1: *Continue to develop typing protocols for non-HLA immunogenetic loci, development of a lab network, enhancement of database to capture non-HLA data and continue analyses to evaluate genetic diversity in the transplant population.*

Period 6 Activity:

- Work with external collaborators has progressed to incorporate an intake method (pipeline) for HLA and KIR data. A solution has been crafted for securely transferring HLA and KIR NGS data between external collaborators and Bioinformatics Research. Computational barriers have been overcome by leveraging internal and external virtualized computer networks.

IID. Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.

IID.1 Task 1: *Conduct observational research and interventional clinical trials.*

Period 6 Activity:

- The CIBMTR completed the preliminary analysis for a study entitled, "Cord blood unit release testing criteria and impact on the transplantation outcome." The primary aim of the study was to determine the impact of CBU CFU testing at the time of release on transplantation outcome. The focus of the study was on the CFU assay because post-thaw growth is indicative of overall unit suitability and approximately 50% of NMDP network CBBs perform the assay pre-release. Preliminary results presented at the International Cord Blood Symposium in June 2014 showed no correlation between post thaw CFU dose and neutrophil engraftment. There was a suggestion that low CFU doses were associated with delayed engraftment by day 28, but the effect disappeared by days 45 and 60 post transplant. The analyses will be finalized in the next several months.

ACRONYM LIST

AABB	American Association of Blood Banks	HRSA	Health Resources and Services Administration
AFA	African American	HSC	Hematopoietic Stem Cell
AGNIS	A Growable Network Information System	IBWC	Immunobiology Working Committee
ABD	Antigen Binding Domain	ICRHER	International Consortium for Research on Health Effects of Radiation
AML	Acute Myelogenous Leukemia	IDM	Infectious Disease Markers
API	Asian Pacific Islander	IHWG	International Histocompatibility Working Group
AQP	Ancestry Questionnaire Project	IPR	Immunobiology Project Results
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IND	Investigational New Drug
ASBMT	American Society for Blood and Marrow Transplantation	IS	Information Services
ASHI	American Society for Histocompatibility and Immunogenetics	IT	Information Technology
ASTHO	Association of State and Territorial Health Officials	IRB	Institutional Review Board
B-LCLs	B-Lymphoblastoid Cell Lines	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BARDA	Biomedical Advanced Research and Development Authority	KIR	Killer Immunoglobulin-like Receptor
BBMT	Biology of Blood and Marrow Transplant	LCL	Lymphoblastoid Cell Line
BCP	Business Continuity Plan	MDACC	MD Anderson Cancer Center
BCPeX	Business Continuity Plan Exercise	MDS	Myelodysplastic Syndrome
BMCC	Bone Marrow Coordinating Center	MHC	Major Histocompatibility Complex
BMDW	Bone Marrow Donors Worldwide	MICA	MHC Class I-Like Molecule, Chain A
BMT	Bone Marrow Transplantation	MICB	MHC Class I-Like Molecule, Chain B
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MKE	Milwaukee
BODI	Business Objects Data Integrator	MRD	Minimal Residual Disease
BRT	Basic Radiation Training	MSKCC	Memorial Sloan-Kettering Cancer Center

C&A	Certification and Accreditation	MSP	Minneapolis
CAU	Caucasian	MUD	Matched Unrelated Donor
CBMTG	Canadian Blood and Marrow Transplant Group	NAC	Nuclear Accident Committee
CBB	Cord Blood Bank	NACCHO	National Association of County & City Health Officials
CBC	Congressional Black Caucus	NCBI	National Center for Biotechnology Information
CBS	Canadian Blood Service	NCBM	National Conference of Black Mayors
CBU	Cord Blood Unit	NARR	National Alliance for Radiation Readiness
CDA	Clinical Document Architecture	NCI	National Cancer Institute
CDE	Common Data Element	NDMS	National Disaster Medical System
CFU	Colony Forming Unit	NEMO	N-locus Expectation-Maximization using Oligonucleotide typing data
CGI	Common Gateway Interface	NGS	Next Generation Sequencing
CHORI	Children's Hospital of Oakland Research Institute	NHLBI	National Heart Lung and Blood Institute
CHTC	Certified Hematopoeitic Transplant Coordinator	NIH	National Institutes of Health
CIBMTR®	Center for International Blood & Marrow Transplant Research	NIMA	Non-Inherited Maternal Antigen
CIT	CIBMTR Information Technology	NIMS	National Incident Management System
CLIA	Clinical Laboratory Improvement Amendment	NK	Natural Killer
CMCR	Centers for Medical Countermeasures Against Radiation	NLE	National Level Exercise
CME	Continuing Medical Education	NMDP®	National Marrow Donor Program
CMF	Community Matching Funds	NRP	National Response Plan
CMV	Cytomegalovirus	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
CNV	Copy Number Variation	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
COG	Children's Oncology Group	OIT	Office of Information Technology
CREG	Cross Reactive Groups	OMB	Office of Management and Budget
CSS	Center Support Services	ONR	Office of Naval Research

CT	Confirmatory Testing	OTTR	Organ Transplant Tracking Record
CTA	Clinical Trial Application	P2P	Peer-to-Peer
		PBMC	Peripheral Blood Mononuclear Cells
DC	Donor Center	PBSC	Peripheral Blood Stem Cell
DHHS-ASPR	Department of Health and Human Service – Assistant Secretary Preparedness and Response	PCR	Polymerase Chain Reaction
DIY	Do it yourself	PHE	Public Health Emergencies
DKMS	Deutsche Knochenmarkspenderdatei	PSA	Public Service Announcement
DMSO	Dimethylsulphoxide	QC	Quality control
DoD	Department of Defense	RCC	Renal Cell Carcinoma
DNA	Deoxyribonucleic Acid	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
DR	Disaster Recovery	REAC/TS	Radiation Emergency Assistance Center/Training Site
D/R	Donor/Recipient	RED	Radiological Exposure Device
DSTU	Draft Standard for Trial Use	REST	Representational State Transfer
EBMT	European Group for Blood and Marrow Transplantation	RFP	Request for Proposal
ED	Emergency Department	RFQ	Request for Quotation
EDC	Electronic Data Capture	RG	Recruitment Group
EFI	European Federation of Immunogenetics	RITN	Radiation Injury Treatment Network
EM	Expectation Maximization	SBT	Sequence Based Typing
EMDIS	European Marrow Donor Information System	SCTOD	Stem Cell Therapeutics Outcome Database
ENS	Emergency Notification System	SG	Sample Group
ERSI	Environment Remote Sensing Institute	SHF	Synthetic Haplotype Frequency
FACT	Federation for the Accreditation of Cellular Therapy	SLCBB	St. Louis Cord Blood Bank
FBI	Federal Bureau of Investigation	SLW	STAR Link® Web
FDA	Food and Drug Administration	SSA	Search Strategy Advice
FDR	Fund Drive Request	SSO	Sequence Specific Oligonucleotides
FEMA	Federal Emergency Management Agency	SSP	Sequence Specific Primers
FLOCK	Flow Cytometry Analysis Component	SSOP	Sequence Specific Oligonucleotide Probes

FP	Filter Paper	STAR®	Search, Tracking and Registry
Fst	Fixation Index	SW	Buccal Swab
GETS	Government Emergency Telecommunications Service	TC	Transplant Center
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	TED	Transplant Essential Data
GIS	Geographic Information System	TIDES	Toolkit for Immunogenomic Data Exchange and Storage
GS	General Services	TNC	Total Nucleated Cell
GTR	Genetic Testing Registry	TP	Time Point
GvHD	Graft vs Host Disease	TSA	Transportation Security Agency
HCS®	HealthCare Standard	UCBT	Umbilical Cord Blood Transplant
HCT	Hematopoietic Cell Transplantation	UCSF	University of California – San Francisco
HEPP	Hospital Emergency Preparedness Program	USID	Unique System Identifier
HHQ	Health History Questionnaire	USIDNet	U.S. Immunodeficiencies Network
HHS	Health and Human Services	UI	User Interface
HIPAA	Health Insurance Portability and Accountability Act	UML	Unified Modeling Language
HIS	Hispanic	URD	Unrelated Donor
HLA	Human Leukocyte Antigen	WGA	Whole Genome Amplification
HML	Histoimmunogenetics Mark-up Language	WMDA	World Marrow Donor Association
HR	High Resolution	WU	Work-up